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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

Takeda Pharmaceutical Company Limited and
Takeda Pharmaceuticals North America, Inc.,

Plaintiffs,

v.

Synthon Pharmaceuticals, Inc. and
Breckenridge Pharmaceutical, Inc.,

Defendants.

Civil Action No.

COMPLAINT

Plaintiffs, Takeda Pharmaceutical Company Limited (formerly known as Takeda Chemical Industries, Ltd.) ("TPC") and Takeda Pharmaceuticals North America, Inc. ("TPNA") (collectively, "Takeda" or "Plaintiffs"), by their undersigned counsel, for their Complaint against defendants Synthon Pharmaceuticals, Inc. ("Synthon") and Breckenridge Pharmaceutical, Inc. ("Breckenridge") (collectively, "the Synthon defendants"), allege as follows:

Jurisdiction and Venue

1. This is an action for patent infringement arising under the patent laws of the United States, Title 35, United States Code and arising under 35 U.S.C. §§ 271(e)(2), 271(b), and 281-283. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a). Venue is proper under 28 U.S.C. §§ 1391(b)-(c) and 1400(b). Personal jurisdiction over the defendants in New York is proper under N.Y. C.P.L.R. §§ 301 and 302(a), and because defendants are doing business in this jurisdiction.

Parties

2. TPC is a Japanese corporation having its corporate headquarters in Osaka, Japan and principal place of business in Osaka, Japan. TPNA is a wholly owned U.S. subsidiary of Takeda American Holdings, Inc., which is a wholly owned U.S. subsidiary of TPC. TPNA has its corporate headquarters and principal place of business in Deerfield, Illinois and is organized under the laws of Delaware.

3. TPC is engaged in the business of research, developing, manufacturing and marketing of a broad spectrum of innovative pharmaceutical products, including ACTOS® which contains the active ingredient pioglitazone.

4. On information and belief, Synthon is a company organized and existing under the laws of North Carolina, having its principal place of business at 9000 Development Drive, Research Triangle Park, North Carolina 27709. Upon information and belief, Synthon filed ANDA No. 78-472 ("Synthon's ANDA") with respect to pioglitazone hydrochloride tablets, 15 mg, 30 mg, and 45 mg ("Synthon's ANDA Product").

5. On information and belief, Breckenridge is a corporation organized and existing under the laws of Florida, having its principal place of business at 1141 South Rogers Circle, Suite 3, Boca Raton, Florida 33487. On information and belief, Breckenridge has an exclusive

agreement with Synthon to distribute Synthon's ANDA Product upon final approval of Synthon's ANDA by the FDA.

6. On information and belief, Synthon is in the business of developing, producing and selling generic pharmaceutical products, which it sells throughout the United States including to and through distributors and other intermediaries throughout the United States.

7. On information and belief, Breckenridge is in the business of research and development, manufacture, marketing and distribution of generic pharmaceutical drugs, throughout the United States, including in at least the Southern District of New York. Further, upon information and belief, Breckenridge has regularly invoked the benefits and protection of the laws of the state of New York by filing lawsuits in federal courts within the state of New York.

8. On information and belief, Breckenridge is currently transacting business in the Southern District of New York, at least by making and shipping into this Judicial District, or by using, offering to sell or selling or by causing others to use, offer to sell or sell, pharmaceutical products. On information and belief, Breckenridge derives substantial revenue from interstate and/or international commerce, including substantial revenue from goods used or consumed or services rendered in the State of New York and this Judicial District. On information and belief, Synthon's exclusive agreement with Breckenridge to distribute Synthon's ANDA Product upon final approval of Synthon's ANDA by the FDA would result in Synthon transacting business in the Southern District of New York, at least by making and shipping its ANDA Product into this Judicial District through Breckenridge, or by using, offering to sell or selling or by causing others to use, offer to sell or sell, pharmaceutical products, including those that are the subject of Synthon's ANDA. By filing its ANDA, Synthon has committed, and unless enjoined, will

continue to commit, a tortious act without the State of New York, which the Synthon defendants expect or should reasonably expect to have consequences in the State of New York.

The New Drug Application

9. TPNA sells pioglitazone-containing drug products under the trade name ACTOS® in the United States pursuant to the United States Food and Drug Administration's approval of a New Drug Application ("NDA") held by TPNA (NDA No. 21-073).

10. ACTOS® is approved for use as an adjunct to diet and exercise to improve glycemic control in patients with Type 2 Diabetes (non-insulin-dependent diabetes mellitus). ACTOS® is indicated for monotherapy. ACTOS® is also indicated for use in combination with a sulfonylurea, metformin, or insulin when diet and exercise plus the single agent does not result in adequate glycemic control.

11. The approval letter for ACTOS®, with approved labeling, was issued by the FDA on July 15, 1999. The approval was for both monotherapy and combination therapy, based upon the FDA's consideration of clinical studies, presented in a single NDA, for both types of therapies.

12. Certain amendments to the approved labeling for ACTOS® have subsequently been approved.

The Patents in Suit

13. United States Patent No. 5,965,584 ("the '584 patent"), entitled "Pharmaceutical Composition," a true and correct copy of which is appended hereto as **Exhibit A**, was duly issued on October 12, 1999 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka and assigned to plaintiff TPC. The '584 patent claims, inter alia, a pharmaceutical composition comprising pioglitazone [(±)-5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-2,4-thiazolidinedione], or salts thereof in combination with a biguanide (e.g., metformin) and

methods for treating diabetes which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with a biguanide.

14. Plaintiff TPC has been and still is the owner through assignment of the '584 patent, which expires on June 19, 2016.

15. United States Patent No. 6,329,404 ("the '404 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as **Exhibit B**, was duly issued on December 11, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '404 patent claims, inter alia, a pharmaceutical composition comprising pioglitazone or salts thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea, such as glimepiride) and methods for treating diabetes which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with an insulin secretion enhancer.

16. Plaintiff TPC has been and still is the owner through assignment of the '404 patent, which expires on June 19, 2016.

17. United States Patent No. 6,166,043 ("the '043 patent"), entitled "Pharmaceutical Composition," a true and correct copy of which is appended hereto as **Exhibit C**, was duly issued on December 26, 2000 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '043 patent claims, inter alia, methods for reducing the amount of active components administered to a diabetic patient, which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with a biguanide, e. g., metformin.

18. Plaintiff TPC has been and still is the owner through assignment of the '043 patent, which expires on June 19, 2016.

19. United States Patent No. 6,172,090 ("the '090 patent"), entitled "Pharmaceutical Composition," a true and correct copy of which is appended hereto as **Exhibit D**, was duly issued on January 9, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '090 patent claims, inter alia, methods for reducing the side effects of active components administered to a diabetic patient, which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with a biguanide, e. g., metformin, as the active components.

20. Plaintiff TPC has been and still is the owner through assignment of the '090 patent, which expires on June 19, 2016.

21. United States Patent No. 6,211,205 ("the '205 patent"), entitled "Pharmaceutical Composition," a true and correct copy of which is appended hereto as **Exhibit E**, was duly issued on April 3, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '205 patent claims, inter alia, methods for reducing the amount of active components administered to a diabetic patient, which comprises administering a therapeutically effective amount of pioglitazone or salts thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea).

22. Plaintiff TPC has been and still is the owner through assignment of the '205 patent, which expires on June 19, 2016.

23. United States Patent No. 6,271,243 ("the '243 patent"), entitled "Pharmaceutical Composition," a true and correct copy of which is appended hereto as **Exhibit F**, was duly issued on August 7, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '243 patent claims, inter alia, methods for reducing the side effects of active components administered to a diabetic patient, which comprises administering a

therapeutically effective amount of pioglitazone or salts thereof in combination with an insulin preparation.

24. Plaintiff TPC has been and still is the owner through assignment of the '243 patent, which expires on June 19, 2016.

25. United States Patent No. 6,303,640 ("the '640 patent"), entitled "Pharmaceutical Composition," a true and correct copy of which is appended hereto as **Exhibit G**, was duly issued on October 16, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '640 patent claims, inter alia, methods for reducing the side effects of active components administered to a diabetic patient, which comprises administering a therapeutically effective amount of a pioglitazone or salt thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea).

26. Plaintiff TPC has been and still is the owner through assignment of the '640 patent, which expires on August 9, 2016.

27. Plaintiff TPC has granted an exclusive license to plaintiff TPNA under the '584 patent, the '404 patent, the '043 patent, the '090 patent, the '205 patent, the '243 patent, and the '640 patent (collectively, the "Takeda Patents").

28. In accordance with its exclusive license, plaintiff TPNA sells pioglitazone-containing drug products under the trade name ACTOS®, among others, in the United States. Sales of TPNA's pioglitazone-containing drug products are made pursuant to approval by the FDA of, among others, NDA No. 21-073.

29. Plaintiff TPC manufactures the ACTOS® drug products sold by TPNA.

30. Plaintiffs TPC and TPNA will be both substantially and irreparably harmed by infringement of any of the Takeda Patents. There is no adequate remedy at law.

COUNT I

(INFRINGEMENT OF THE '584 PATENT UNDER 35 U.S.C. § 271(E)(2)(A))

31. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

32. Upon information and belief, Synthon filed an Abbreviated New Drug Application ("ANDA") with the Food and Drug Administration ("FDA") under 21 U.S.C. § 355(j) (ANDA No. 78-472) seeking approval to market Synthon's ANDA Product. Upon information and belief, Breckenridge will be the exclusive distributor in the United States of Synthon's ANDA Product.

33. By this ANDA filing and distribution agreement, the Synthon defendants have indicated that they intend to engage, and that there is substantial likelihood that they will engage, in the commercial manufacture, use, and/or sale, or inducement thereof, of plaintiffs' patented pioglitazone drug products immediately or imminently upon receiving FDA approval to do so. Also by this ANDA filing, Synthon has indicated that Synthon's ANDA Product is bioequivalent to Takeda's pioglitazone drug products.

34. By this ANDA filing, Synthon seeks to obtain approval to commercially manufacture, use, import, offer for sale, and/or sell, alleged generic equivalents of plaintiffs' ACTOS® pioglitazone drug products prior to the expiration date of the '584 patent.

35. By a letter (the "Notice Letter") dated July 30, 2010, Synthon informed TPC and TPNA that Synthon had filed a certification to the FDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV). On or about August 2, 2010, NDA holder, TPNA, received the Notice Letter. On or about August 2, 2010, patent owner, TPC, received a duplicate original of the Notice Letter.

36. The Notice Letter, purporting to be Synthon's Notice of Certification under 21 U.S.C. § 355(j)(2)(B)(ii)-(iv), indicates that Synthon intends to manufacture, use, and/or sell, a pioglitazone hydrochloride tablet drug product prior to the expiration of the '584 patent. The Notice Letter alleges that in Synthon's opinion, the '584 patent is "invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of Synthon's proposed drug product."

37. Synthon's filing of ANDA No. 78-472 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, and/or sale, or inducement thereof, of drug products containing pioglitazone or salts thereof before the expiration of the '584 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

38. The Synthon defendants' manufacture, use, and/or sale, or inducement thereof, of Synthon's ANDA Product will induce infringement of at least one claim of the '584 patent under 35 U.S.C. § 271(e)(2)(A).

39. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in combination therapy, and that such use does not require a physician to co-prescribe pioglitazone with a biguanide, e.g., metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to customers of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

40. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with

pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

41. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides, e.g., metformin, and such information will promote the use of pioglitazone in combination with biguanides, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

42. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and metformin, a biguanide, also applies to Synthon's ANDA Product.

43. Upon information and belief, the Synthon defendants have planned and intend to actively induce others to infringe the '584 patent when Synthon's ANDA application is approved and plan and intend to do so on approval.

44. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful, and in full knowledge of the existence of the '584 patent.

45. Unless the Synthon defendants are enjoined from infringing and inducing the infringement of the '584 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT II

(INFRINGEMENT OF THE '404 PATENT UNDER 35 U.S.C. § 271(E)(2)(A))

46. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

47. Synthon's Notice Letter, purporting to be Synthon's Notice of Certification under 21 U.S.C.§ 355(j)(2)(B)(ii)-(iv), also indicates that Synthon intends to manufacture, use, and/or sell a pioglitazone hydrochloride tablet drug product prior to the expiration of the '404 patent. The Notice Letter alleges that in Synthon's opinion, the '404 patent is "invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of Synthon's proposed drug product."

48. Synthon's filing of ANDA No. 78-472 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, and/or sale, or inducement thereof, of drug products containing pioglitazone or salts thereof before the expiration of the '404 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

49. The Synthon defendants' manufacture, use, and/or sale, or inducement thereof, of Synthon's ANDA Product will induce infringement of at least one claim of the '404 patent under 35 U.S.C. § 271(e)(2)(A).

50. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in combination therapy to treat diabetes, and that such use does not require a physician to co-prescribe pioglitazone with an insulin secretion enhancer (e.g., a sulfonylurea). Further, patients routinely take pioglitazone in combination with additional active components, such as insulin secretion enhancers. The intended use of pioglitazone in combination therapy would be readily apparent to customers of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

51. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

52. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin secretion enhancers such as a sulfonylurea and such information will promote the use of pioglitazone in combination with insulin secretion enhancers such as a sulfonylurea. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. The Synthon defendants knows or reasonably should know that their proposed conduct will induce infringement.

53. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Synthon's ANDA Product.

54. Upon information and belief, the Synthon defendants have planned and intend to actively induce others to infringe the '404 patent when Synthon's ANDA application is approved and plan and intend to do so on approval.

55. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful, and in full knowledge of the existence of the '404 patent.

56. Unless the Synthon defendants are enjoined from infringing and inducing the infringement of the '404 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT III

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '584 PATENT UNDER 35 U.S.C. § 271(b))

57. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

58. Upon information and belief, approval of ANDA 78-472 is substantially likely to result in the commercial manufacture, use, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a method claimed in one or more claims of the '584 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '584 patent.

59. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '584 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with a biguanide, e.g., metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides for use in methods covered by the '584 patent. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to a customer of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

60. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to

Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

61. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides, and such information will promote the use of pioglitazone in combination with biguanides, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

62. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing

information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and a biguanide, e.g., metformin, also applies to Synthon's ANDA Product.

63. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

64. Unless the Synthon defendants are enjoined from infringing and inducing infringement of the '584 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IV

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '404 PATENT UNDER 35 U.S.C. § 271(b))

65. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

66. Upon information and belief, approval of ANDA 78-472 is substantially likely to result in the commercial manufacture, use, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a method claimed in the '404 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '404 patent.

67. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '404 patent and that use in such method does not require a physician to co-prescribe pioglitazone with an insulin secretion enhancer (e.g., a sulfonylurea). Further, patients routinely take pioglitazone in combination with additional active components, such as insulin secretion enhancers for use in methods covered by the '404 patent. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to a customer of the Synthon defendants (e.g., including,

without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

68. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

69. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin secretion enhancers such as a sulfonylurea and such information will promote the use of pioglitazone in combination with an insulin secretion enhancer, such as a sulfonylurea. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. The Synthon defendants knows or reasonably should know that their proposed conduct will induce infringement.

70. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Synthon's ANDA Product.

71. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

72. Unless the Synthon defendants are enjoined from infringing and inducing infringement of the '404 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT V

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '043 PATENT UNDER 35 U.S.C. § 271(b))

73. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

74. Upon information and belief, approval of ANDA 78-472 is substantially likely to result in the commercial manufacture, use, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a method claimed in one or more claims of the '043 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '043 patent.

75. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '043 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with a

biguanide, e.g., metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides for use in methods covered by the '043 patent. The intended use of pioglitazone in combination therapy to reduce the amount of active components used in such therapy would be readily apparent to a customer of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

76. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '043 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

77. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides, e.g., metformin and such information will promote the use of pioglitazone in combination with biguanides, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known

to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '043 patent. The Synthon defendants knows or reasonably should know that their proposed conduct will induce infringement.

78. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and a biguanide, e.g., metformin, also applies to Synthon's ANDA Product.

79. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

80. Unless the Synthon defendants are enjoined from infringing and inducing infringement of the '043 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VI

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '090 PATENT UNDER 35 U.S.C. § 271(b))

81. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

82. Upon information and belief, approval of ANDA 78-472 is substantially likely to result in the commercial manufacture, use, and/or sale of a drug product which is marketed and sold for use in a method claimed in one or more claims of the '090 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '090 patent.

83. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '090 patent, and that use in such methods does not require a physician to co-prescribe pioglitazone with a biguanide, e.g., metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides for use in methods covered by the '090 patent. The intended use of pioglitazone in combination therapy to reduce side effects of such therapy would be readily apparent to a customer of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

84. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '090 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

85. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides, e.g., metformin

and such information will promote the use of pioglitazone in combination with biguanides, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '090 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

86. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and a biguanide, e.g., metformin, also applies to Synthon's ANDA Product.

87. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

88. Unless the Synthon defendants are enjoined from infringing and inducing infringement of the '090 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VII

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '205 PATENT UNDER 35 U.S.C. § 271(b))

89. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

90. Upon information and belief, approval of ANDA 78-472 is substantially likely to result in the commercial manufacture, use, and/or sale, or inducement thereof, of a drug product

which is marketed and sold for use in a method claimed in one or more claims of the '205 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '205 patent.

91. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '205 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with an insulin secretion enhancer (e.g., a sulfonylurea). Further, patients routinely take pioglitazone in combination with additional active components, such as insulin secretion enhancers for use in methods covered by the '205 patent. The intended use of pioglitazone in combination therapy to reduce the amount of active components used in such therapy would be readily apparent to a customer of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

92. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and

abet, infringement of the '205 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

93. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin secretion enhancers such as a sulfonylurea and such information will promote the use of pioglitazone in combination with insulin secretion enhancers. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '205 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

94. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Synthon's ANDA Product.

95. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

96. Unless the Synthon defendants are enjoined from infringing and inducing infringement of the '205 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VIII

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '243 PATENT UNDER 35 U.S.C. § 271(b))

97. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

98. Upon information and belief, approval of ANDA 78-472 is substantially likely to result in the commercial manufacture, use, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a methods claimed in one or more claims of the '243 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '243 patent.

99. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '243 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with an insulin preparation. Further, patients routinely take pioglitazone in combination with additional active components, such as insulin preparations for use in methods covered by the '243 patent. The intended use of pioglitazone in combination therapy to treat a diabetic patient to reduce side effects of active components used in such therapy would be readily apparent to a customer of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

100. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain

treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '243 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

101. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin preparations, and such information will promote the use of pioglitazone in combination with insulin preparations. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '243 patent. The Synthon defendants knows or reasonably should know that their proposed conduct will induce infringement.

102. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin preparation, also applies to Synthon's ANDA Product.

103. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

104. Unless the Synthon defendants are enjoined from infringing and inducing infringement of the '243 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IX

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '640 PATENT UNDER 35 U.S.C. § 271(b))

105. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

106. Upon information and belief, approval of ANDA 78-472 is substantially likely to result in the commercial manufacture, use, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a methods claimed in one or more claims of the '640 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '640 patent.

107. Upon information and belief, Synthon is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '640 patents and that use in such methods does not require a physician to co-prescribe pioglitazone with an insulin secretion enhancer (e.g., a sulfonylurea). Further, patients routinely take pioglitazone in combination with additional active components, such as insulin secretion enhancers for use in methods covered by the '640 patent. The intended use of pioglitazone in combination therapy to reduce side effects of active components used in such therapy would be readily apparent to a customer of the Synthon defendants (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

108. Upon information and belief, Synthon's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Synthon and customers of the Synthon defendants, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or treatment in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Synthon and customers of the Synthon defendants. On information and belief, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '640 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

109. Additionally, upon information and belief, Synthon's proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin secretion enhancers such as a sulfonylurea and that such information will promote the use of pioglitazone in combination with an insulin secretion enhancer. The beneficial effects of such co-administration and/or interactions are well known to customers of the Synthon defendants. By the inclusion of this information in Synthon's ANDA Product label, the Synthon defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '640 patent. The Synthon defendants know or reasonably should know that their proposed conduct will induce infringement.

110. Upon information and belief, the Synthon defendants intend to refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are

substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Synthon's ANDA Product.

111. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

112. Unless the Synthon defendants are enjoined from infringing and inducing infringement of the '640 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

WHEREFORE, Plaintiffs request the following relief:

(a) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. that making, using, selling, offering to sell and/or importing Synthon's ANDA Product for which it seeks FDA approval or its active ingredient pioglitazone will infringe at least one claim of one or more of the Takeda Patents;

(b) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. that inducing the making, using, offering for sale, selling and/or importing of Synthon's ANDA Product or its active ingredient pioglitazone, will infringe at least one claim of one or more of the Takeda Patents;

(c) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. and an order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any FDA approval for the Synthon defendants to commercially make, use, sell, offer to sell or import pioglitazone or any drug product containing pioglitazone be no

earlier than the date following the expiration date of the last to expire of the Takeda Patents (as extended, if applicable);

(d) a permanent injunction restraining and enjoining against any infringement by defendants, their officers, agents, attorneys, employees, successors or assigns, or those acting in privity or concert with them, of the Takeda Patents, through the commercial manufacture, use, sale, offer for sale or importation into the United States of pioglitazone or any drug product containing pioglitazone, and/or any inducement of the same;

(e) Attorneys' fees in this action under 35 U.S.C. § 285; and

(f) Such further and other relief in favor of Plaintiffs and against Defendants as this Court may deem just and proper.

Dated: New York, New York
September 8, 2010

Takeda Pharmaceutical Company Limited and
Takeda Pharmaceuticals North America, Inc.

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